

FIGURE 1

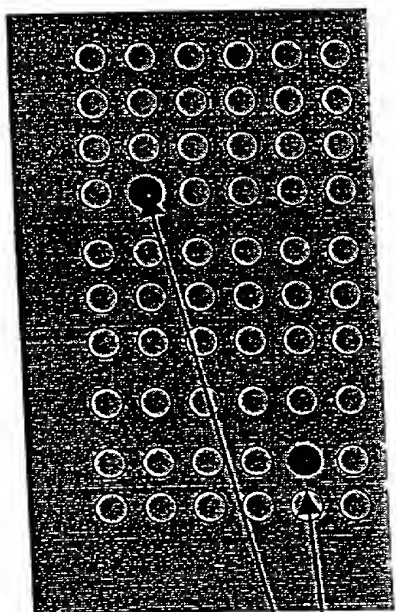
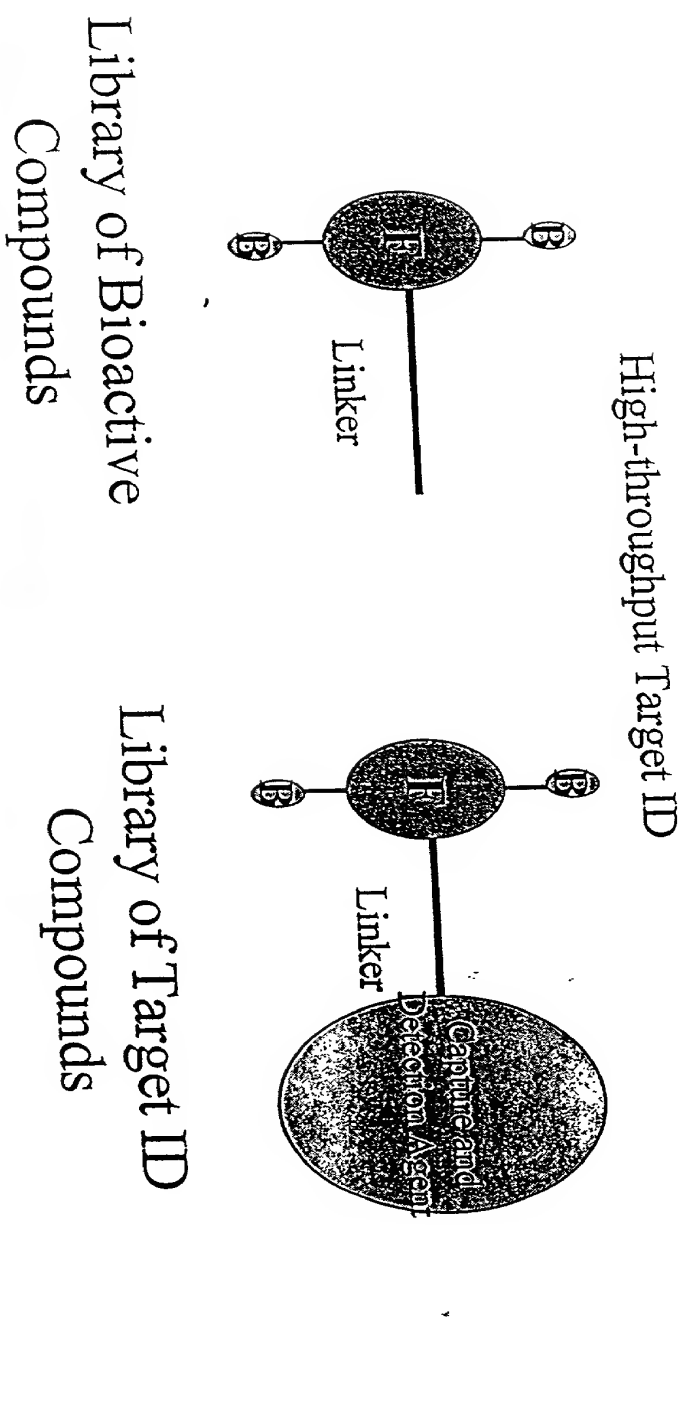
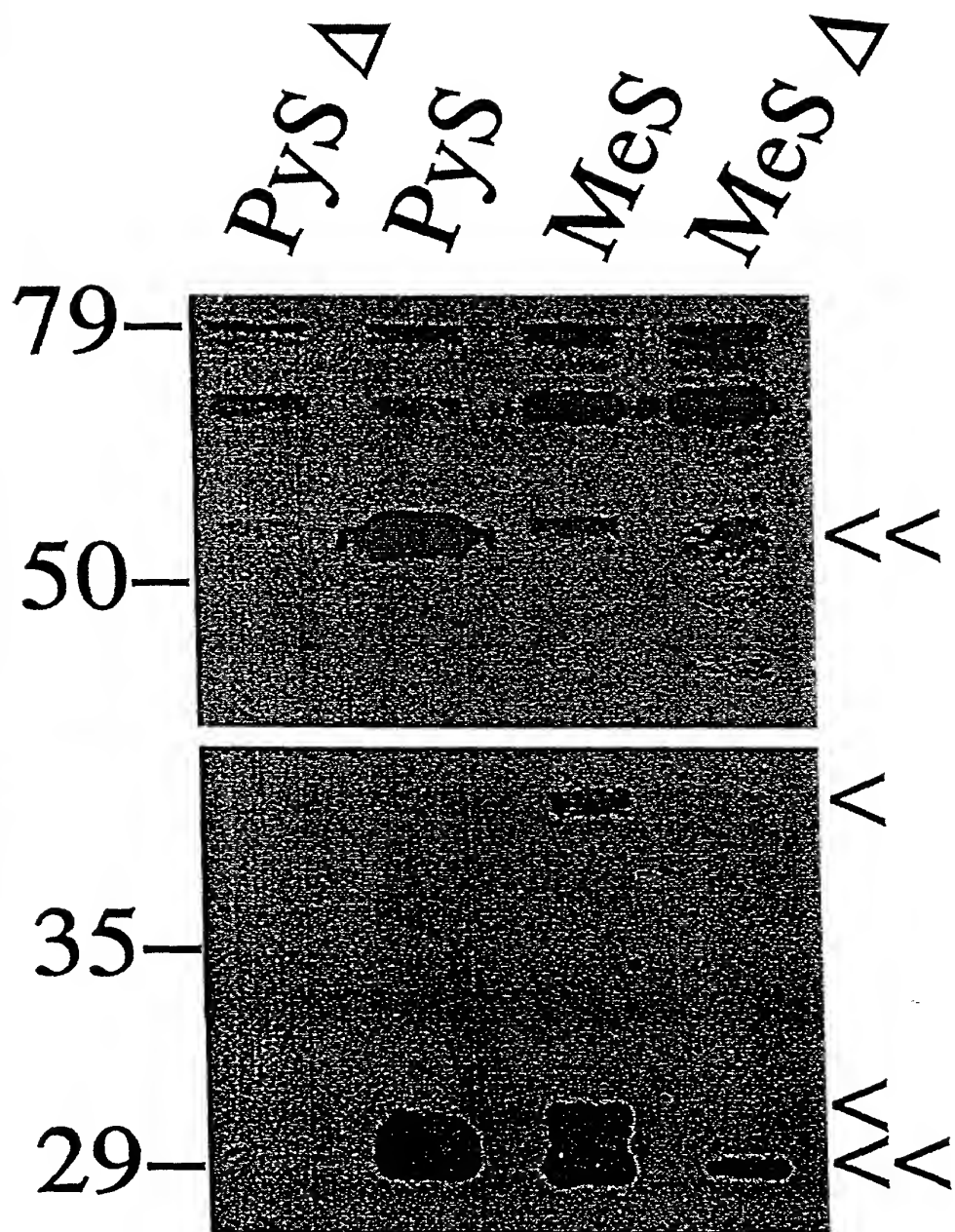
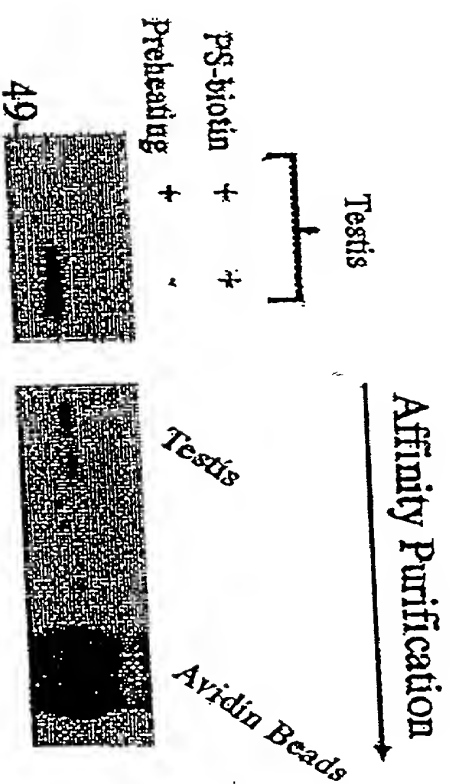
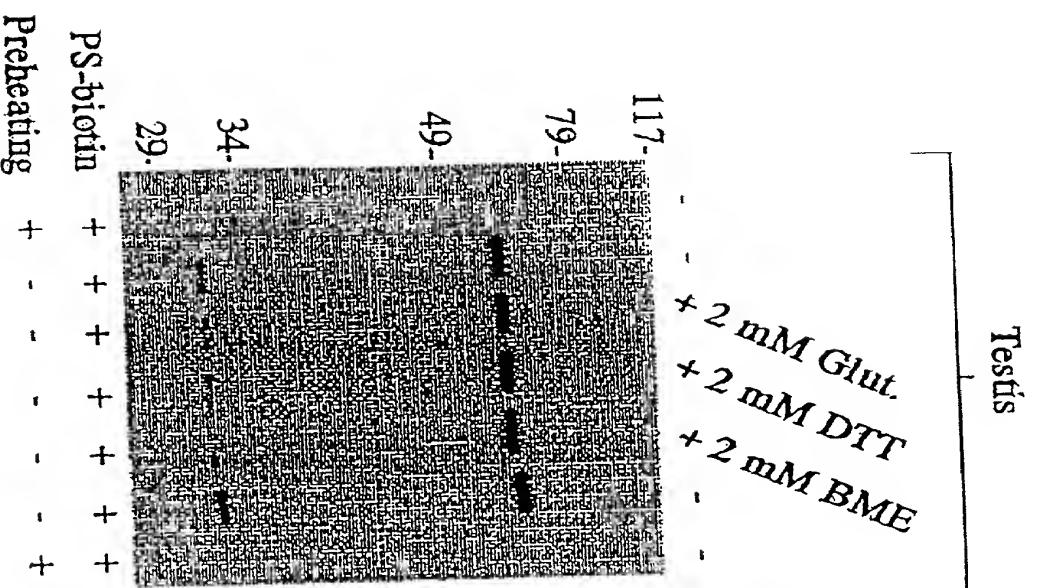


FIGURE 2



Non-Directed Tagged Library of Sulfonates Identifies Probe for ADH Superfamily of Enzymes

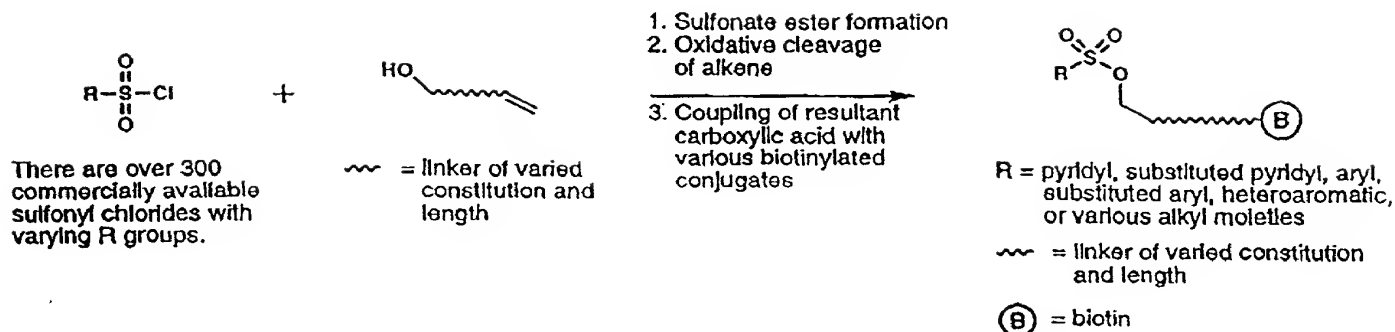


- MALDI mapping identifies tagged protein as aldehyde dehydrogenase (ADH, cytosolic class II)

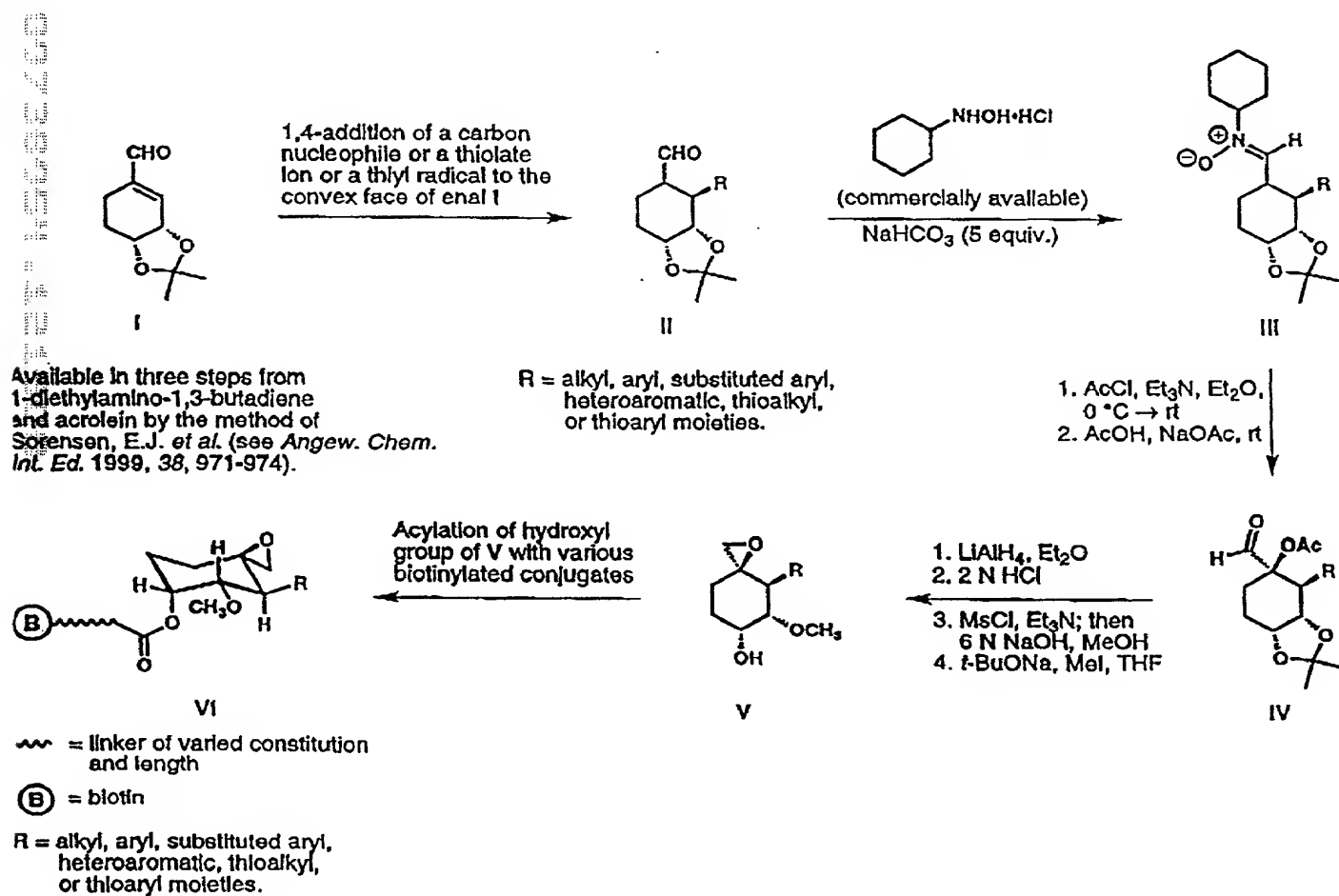
- 28 ADHs in fly genome
 - Involved in retinoic acid biosynthesis and catabolism of alcohol and chemotherapeutic agents

FIGURE 3

FIGURE 4



Scheme 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for I \rightarrow II \rightarrow III \rightarrow IV \rightarrow V can be found in Sorensen, E.J. *et al.* *Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the metalloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

FP-Biotin: a kinetic reporter of SH Activity

- The rates at which the majority of SHs react with FP-biotin can be experimentally followed
- FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes

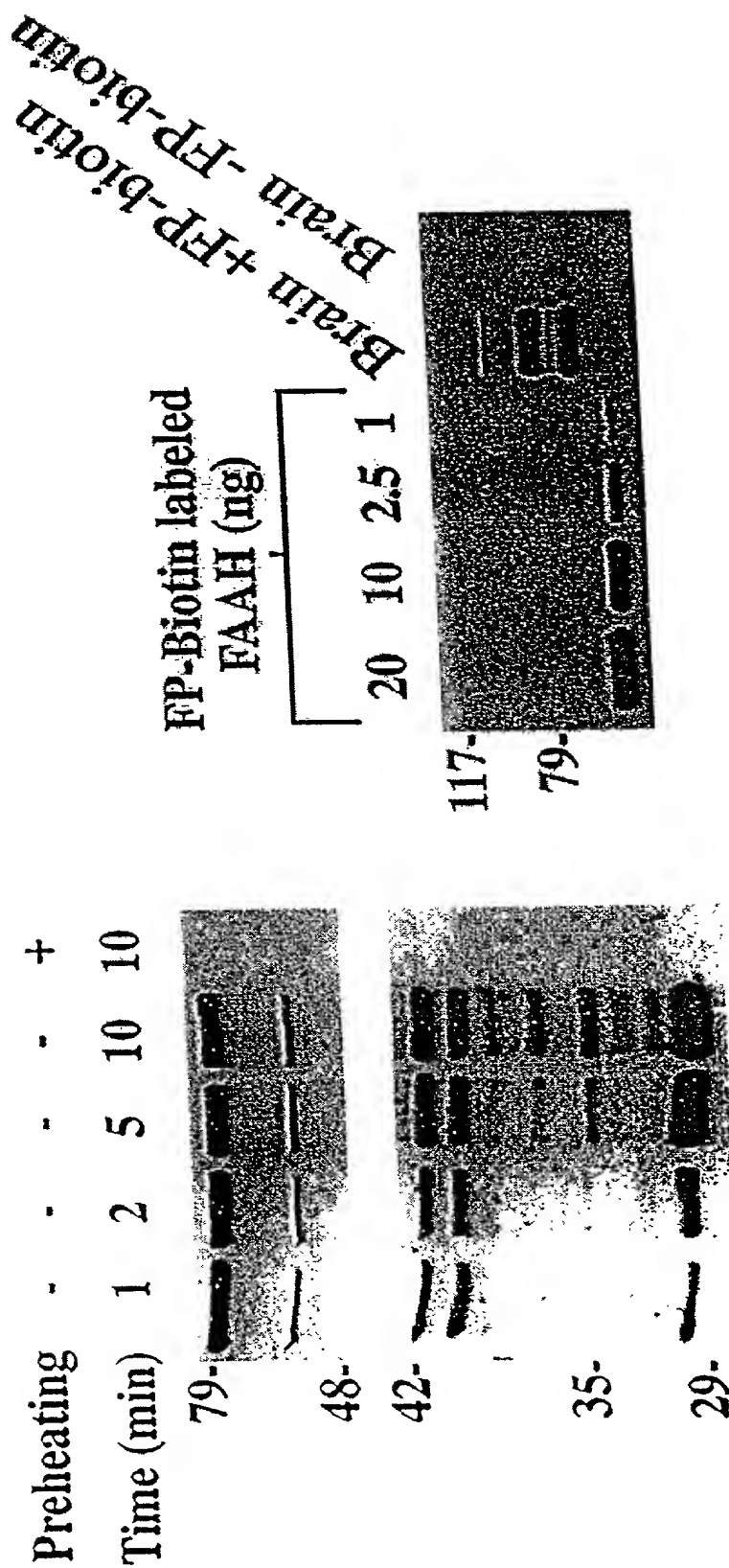


FIGURE 5

Utility of Multiplexed probes in identifying Serine Hydrolases

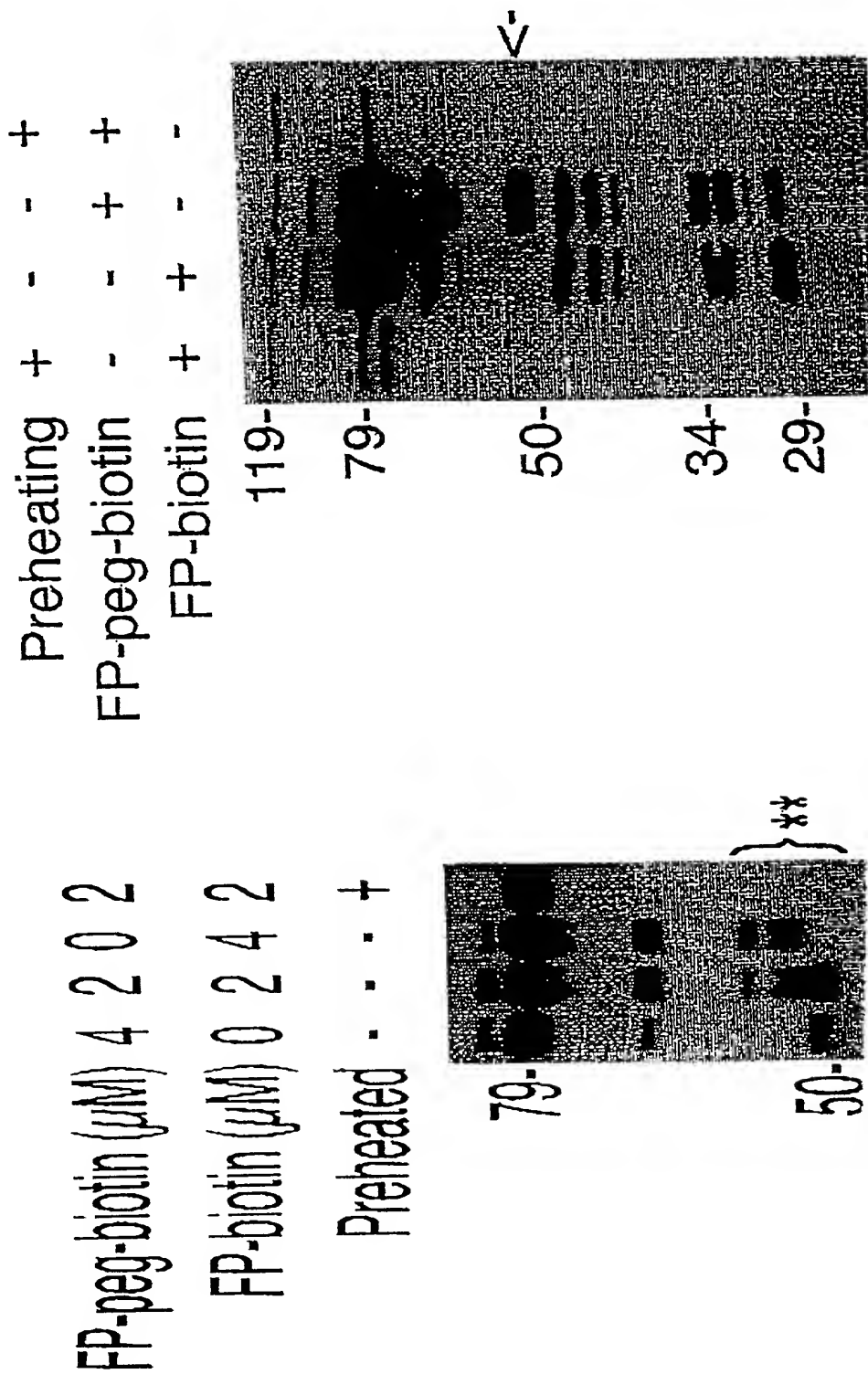
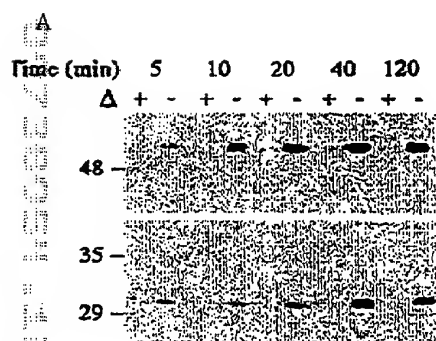


FIGURE 6

FIGURE 7



B

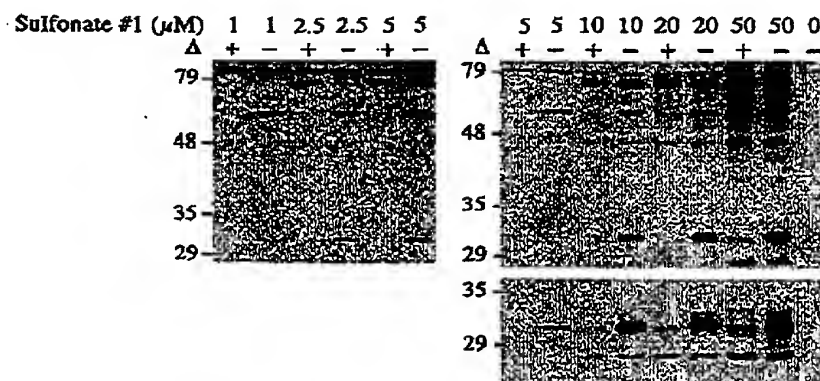
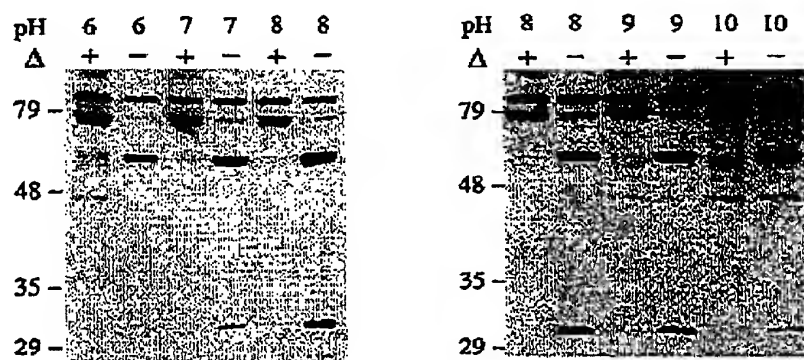
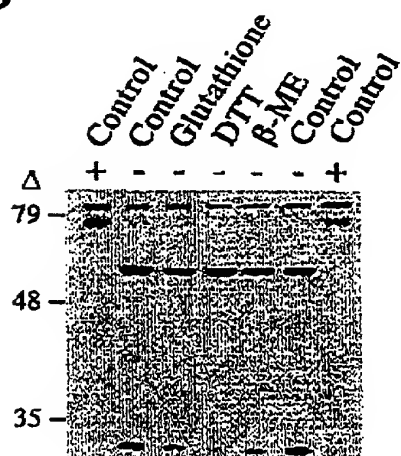


FIGURE 7

C



D



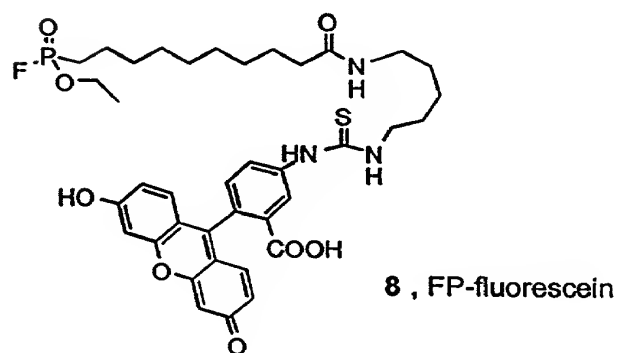
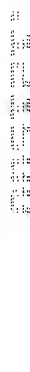
[illegible]

FIGURE 9

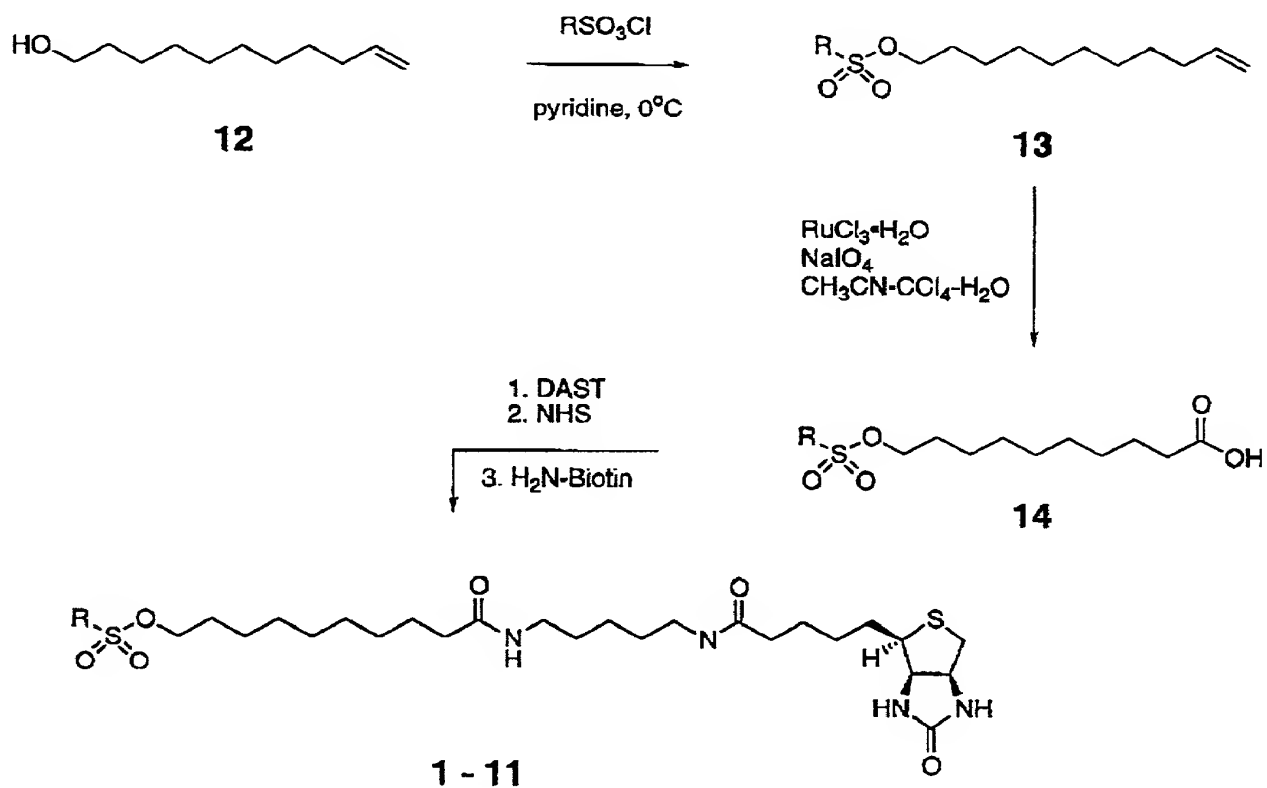
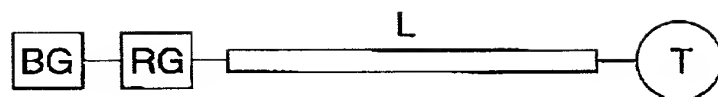


FIGURE 10

A.



B.

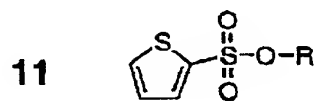
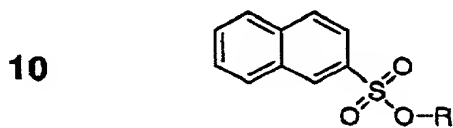
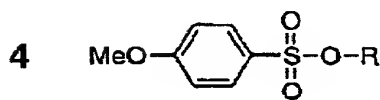
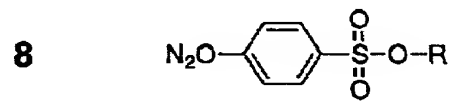
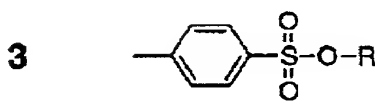
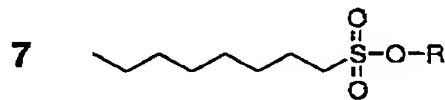
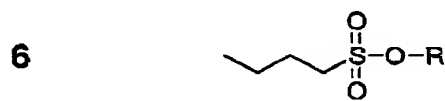
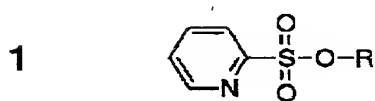
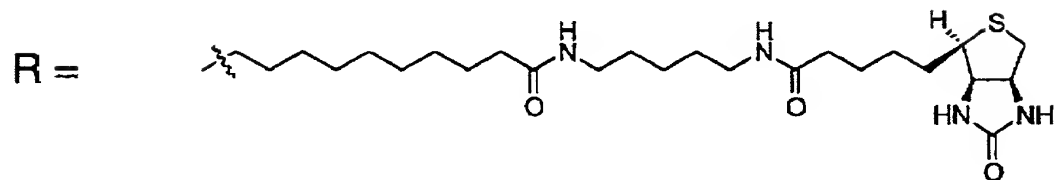
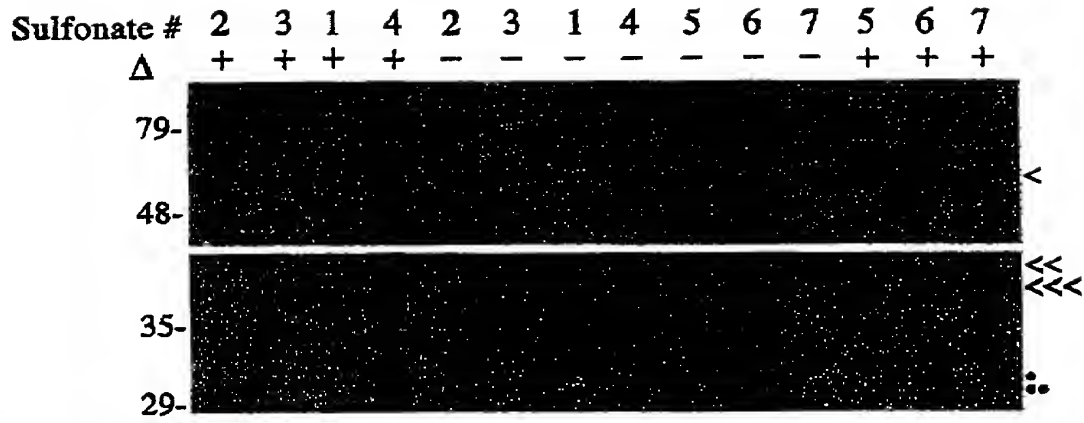


FIGURE 11

A



B

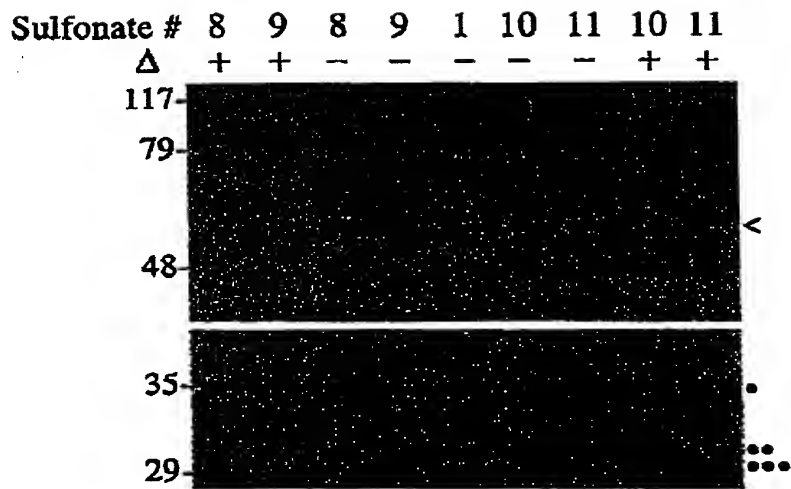


FIGURE 12

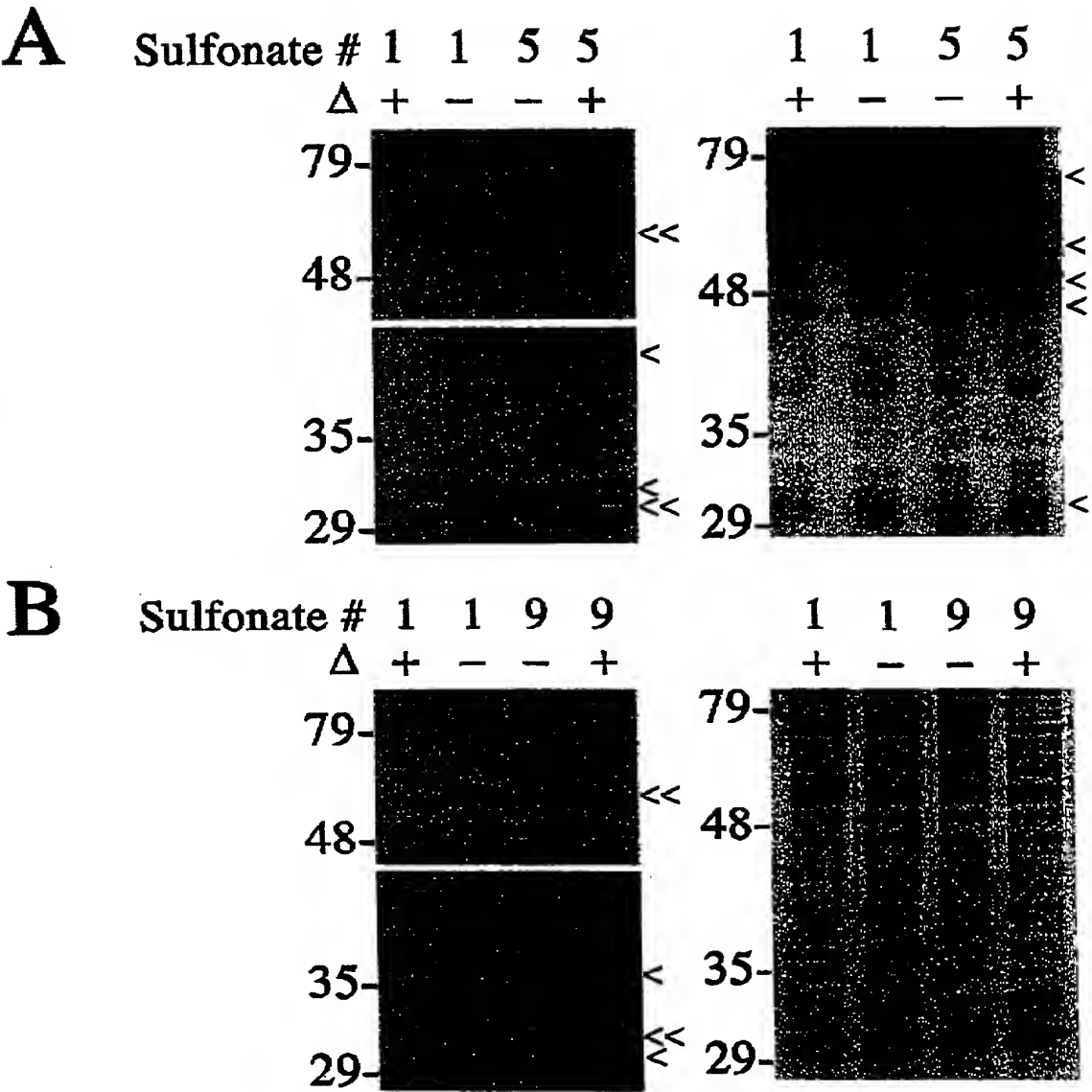
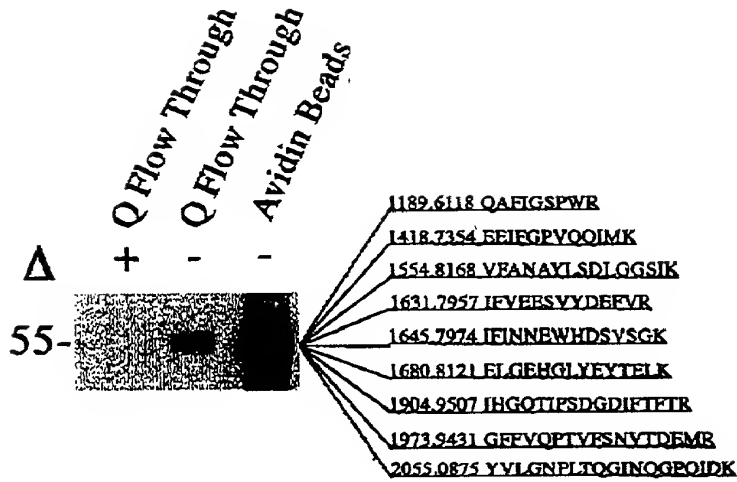
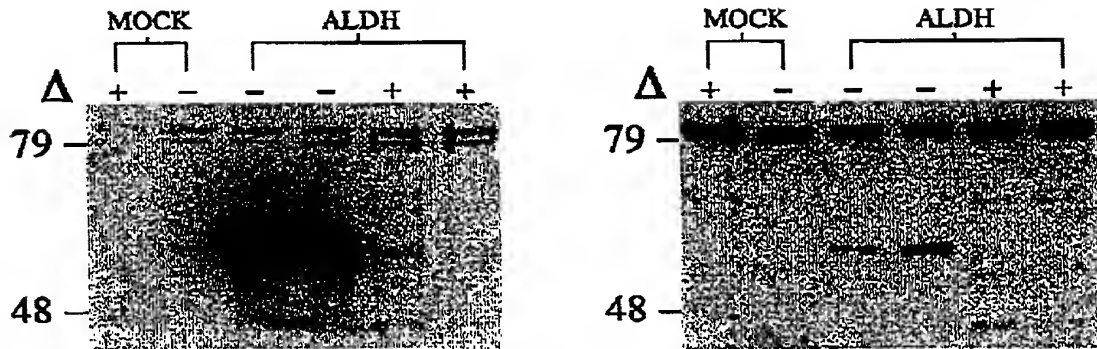


FIGURE 13

A



B



C

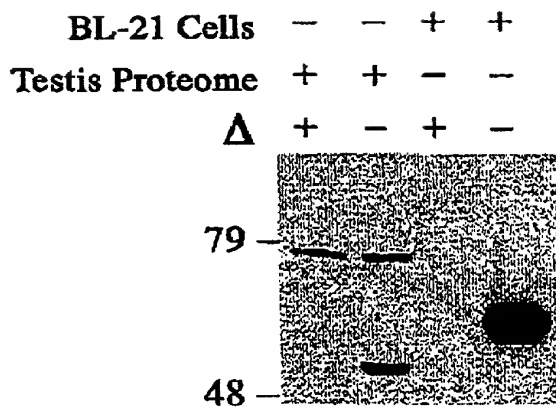
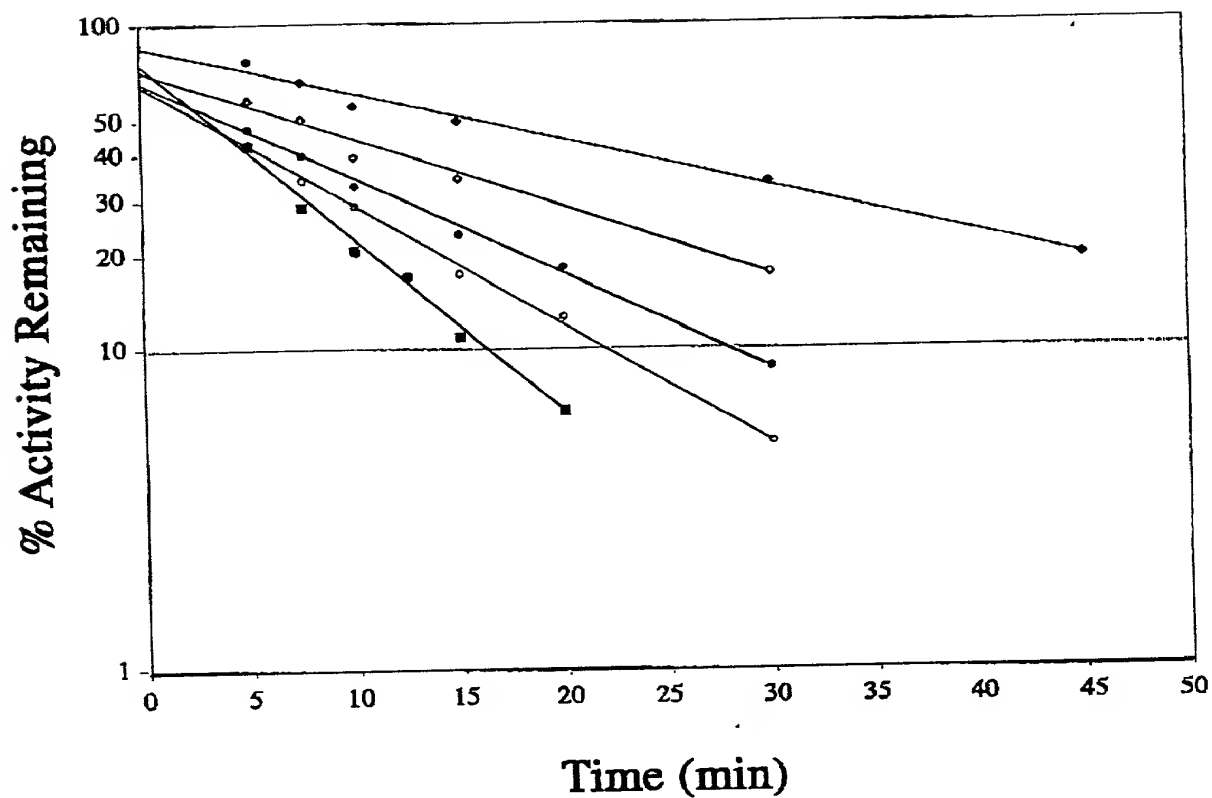


FIGURE 14

A



B

Competitor #	-	-	15	17	16	15	17	16
[Competitor (μ M)]	0	0	5	5	5	50	50	50
Δ	+	-	-	-	-	-	-	-

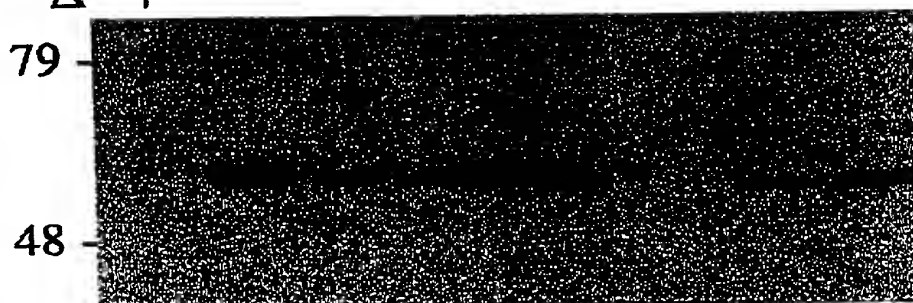


FIGURE 15

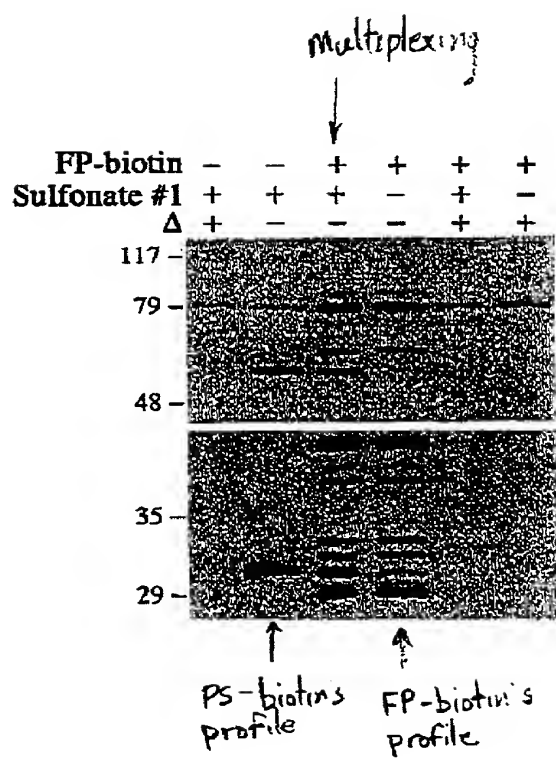


FIGURE 16

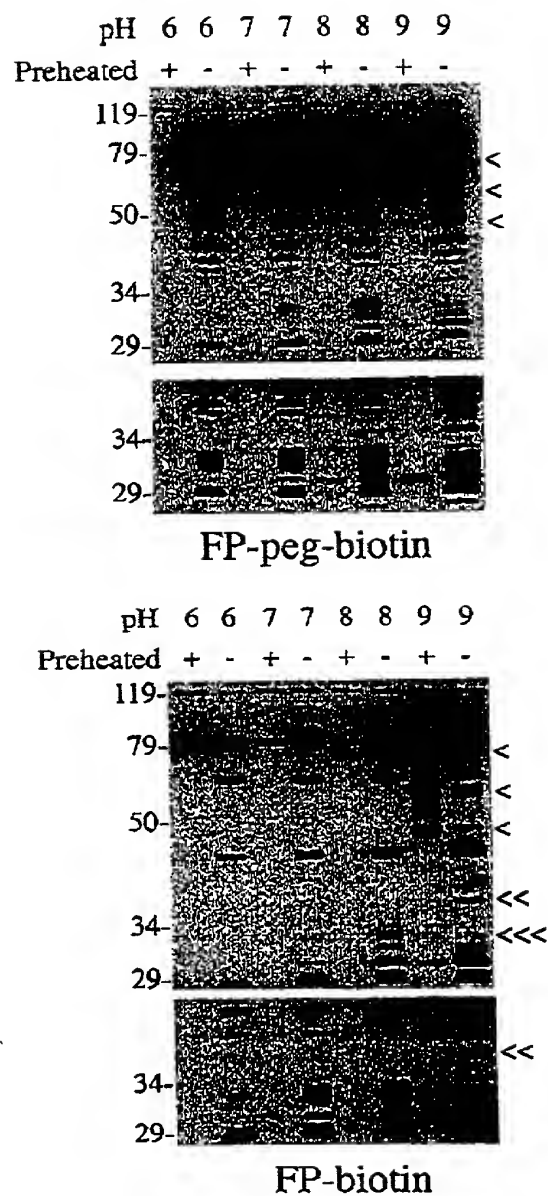


FIGURE 17

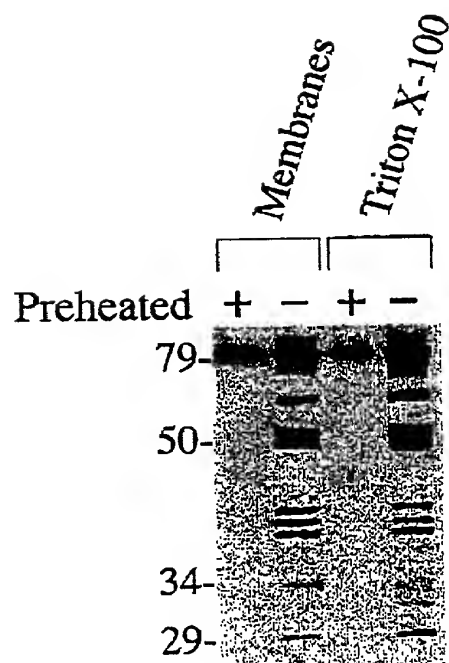


FIGURE 18

FP-peg-biotin	+	+	+	+	+	+	-	-	-
FP-biotin	-	-	-	-	-	-	+	+	+
OTFMK	0	0	200	50	5	1	0	200	50
Δ	+	-	-	-	-	-	-	-	-

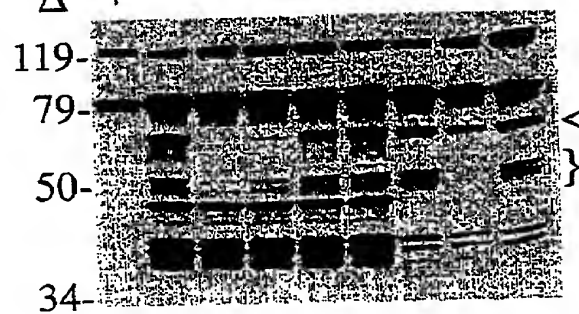


FIGURE 19

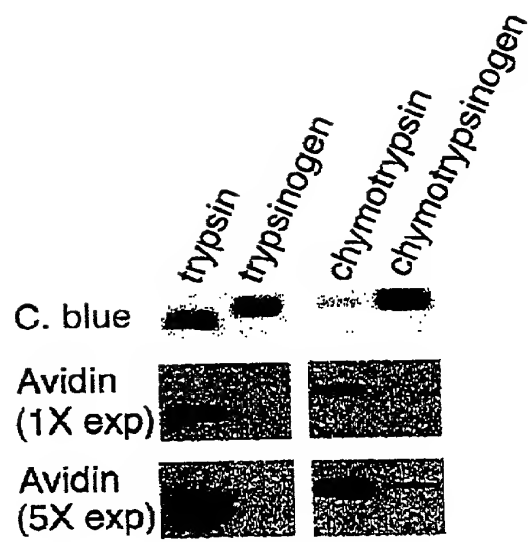
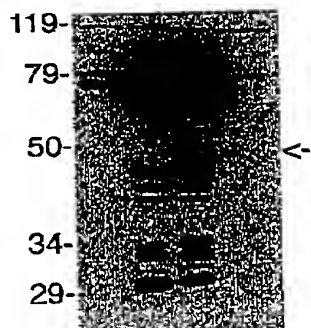


FIGURE 20

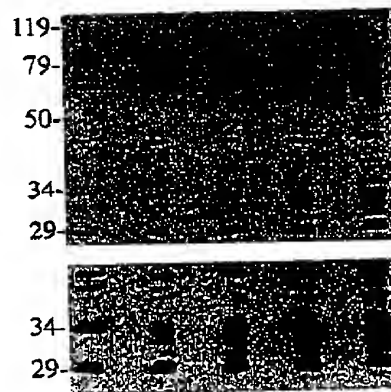
A

FP-peg-biotin	-	-	+	+
FP-biotin	+	+	-	-
Preheated	+	-	-	+



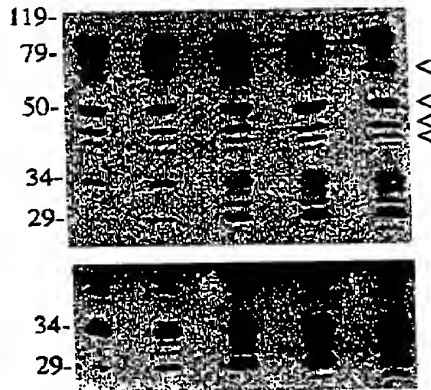
B

FP-biotin (μ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



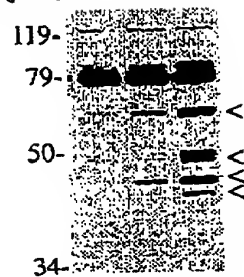
C

FP-peg-biotin (μ M)	0.5	1	1	2	2	4	4	8	8
Preheated	-	+	-	+	-	+	-	+	-



D

FP-peg-biotin (μ M)	1	2	8
--------------------------	---	---	---



One minute
reaction

FIGURE 21

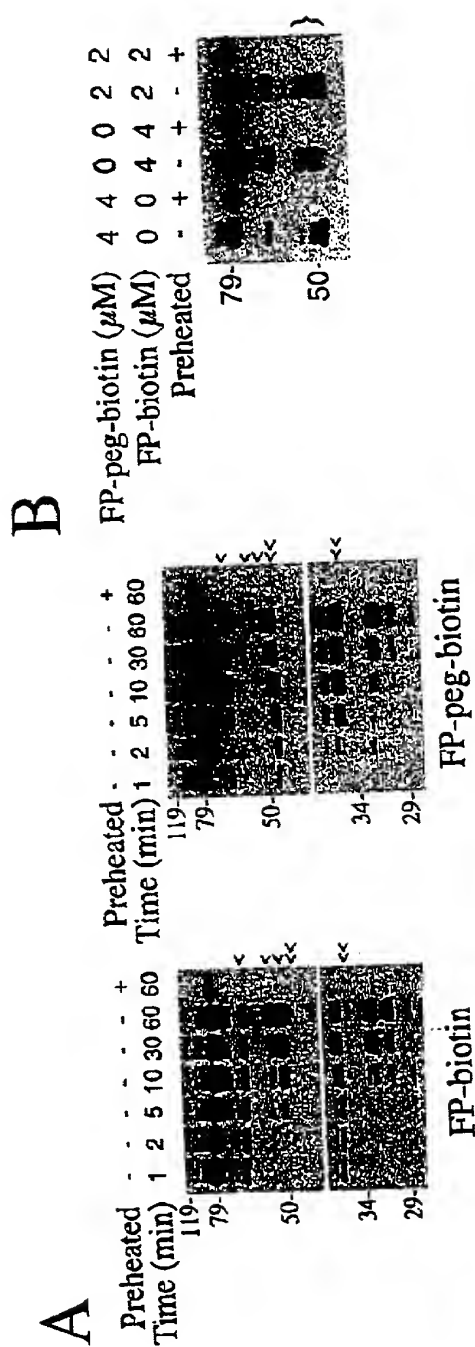


FIGURE 22

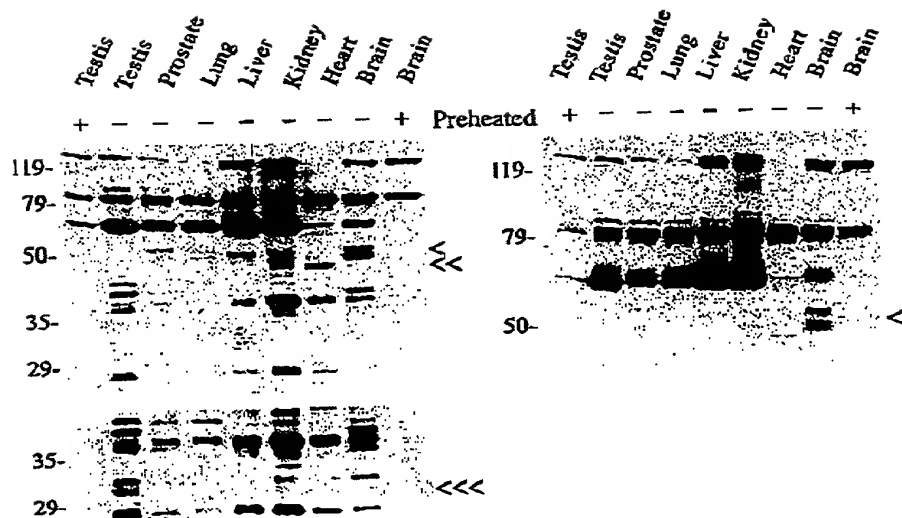


FIGURE 23

